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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,178	01/11/2002	Noriyuki Kasahara	06666-022002	7589
20985 7590 08/24/2007 FISH & RICHARDSON, PC P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022			EXAMINER POPA, ILEANA	
			ART UNIT 1633	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/045,178	Applicant(s) KASAHARA ET AL.	
	Examiner Ileana Popa	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 June 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 41-46, 49-51, 56, 59, 61, 63-73, 75, 77-82 and 87-96 is/are pending in the application.
 4a) Of the above claim(s) 46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 41-45, 49-51, 56, 59, 61, 63-73, 75, 77-82 and 87-96 is/are rejected.
- 7) ☒ Claim(s) 51 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1633

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

2. Claims 1-40, 47, 48, 52-55, 57, 60, 62, 74, 76, and 83-86 have been cancelled. Claim 46 has been withdrawn. Claim 59 has been amended.

Claims 41-45, 49-51, 56, 59, 61, 63-73, 75, 77-82, and 87-96 are under examination.

Response to Arguments

Claim Objections

3. Claim 51 remains objected to under 37 CFR 1.75(c) as being in improper form because it is dependent from the subsequent claim 64.

Applicant argues that there is nothing requiring that a claim depend from a previously numbered claim. In response to this argument, Applicant is directed to 37 C.F.R. 1.75 (c) that states that the dependent claims must "refer back" to another claim or claims (i.e., refer to a previous claim). With respect to Applicant requests that the objection be withdrawn with the understanding that the Examiner will re-number and re-order the claims as necessary upon allowance, it is noted that the claims are not allowable (see below).

Claim Rejections - 35 USC § 112, 2nd paragraph

Art Unit: 1633

4. The rejection of claims 41, 58, and 59 under 35 U.S.C. 112, second paragraph, as being indefinite, is withdrawn in response to Applicant's amendment to the claims filed on 06/08/2007.

Claim Rejections - 35 USC § 112, enablement

5. Claims 41-44, 49-5156, 58, 59, 61, 63-73, 75, 77-82, and 87-96 remain rejected under 35 U.S.C. 112, first paragraph, for the reasons of record set forth in the non-final Office action of 04/10/2007. Applicant's arguments filed 06/08/2007 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that Meng et al. states that intravascular administration may be advantageous if the virus target is the liver, i.e., the intravascular administration is useful in certain situations. Applicant argues that the enablement is not necessarily defeated by the need for some experimentation to determine the properties of a claimed product and the fact that the experimentation may be complex does not necessarily makes it undue, if the art typically engages in such experimentation. Applicant argues that one of skill in the art typically engages in systemic administration of viruses, as evidenced by Meng et al, and that Applicant does not need to demonstrate that the invention is completely safe. Applicant submits that one of skill in the art would be able to administer a retrovirus systemically. Applicant concludes that the claims are enabled and requests the withdrawal of the rejection.

Applicant's arguments are acknowledged, however, the rejection is maintained for the following reasons:

While it is true that the art teaches routine systemic administration of viruses, this is in context of treatment of diseases other than proliferative diseases, such as vaccination to treat infections by pathogens. The art clearly teaches that intravascular administration is not adequate for treating proliferative disorders such as cancer because (i) it dilutes the virus and only a small portion reaches the tumor, (ii) elicits a powerful immune response, (iii) tropism for organs such as the liver can be a disadvantage if delivery is intended elsewhere (see Meng et al.), and (iv) the virus must traverse the endothelial wall and travel against pressures within an expanding tumor mass. Even if Meng et al. teach that intravascular administration may be useful when the target is the liver, this does not mean that this would result in treatment, especially that Meng et al. teach that the virus elicits a powerful immune response. It is also noted that the instant claims are broadly drawn to any proliferative disease of any tissue/organ. Applicant did not provide any example that routes, other than intratumoral delivery, result in treatment of any proliferative disease. Based on the teachings in the art, one of skill in the art would not recognize that routes of delivery other than intratumoral would result in successful therapy (see also the non-final Office action of 04/10/2007).

Claim Rejections - 35 USC § 103

6. Claims 41-45, 49-51, 56, 61, 66, 70, 71, 73, 75, 77-80, 87, 89, and 91 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Ram et al. (Cancer Research, 1993, 53: 83-88), in view of both Martuza (Nature Medicine, 1997, 3: 1323)

and Martuza et al. (U.S. patent No. 5,585,096) for the reasons of record set forth in the non-final Office action of 04/10/2007. Applicant's arguments filed 06/08/2007 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that the Examiner did not establish a *prima facie* case of obviousness. Applicant argues that Ram teaches gene delivery by using a replication defective virus, Martuza teaches replication competent adenoviral and HSV vectors, and the '096' patent teaches a replication competent HSV vector. Applicant points out that adenoviruses and HSV are DNA viruses, while retroviruses, as claimed, are RNA viruses and therefore, absent the instant disclosure, one of skill in the art would not have known how to modify a retrovirus in order to make it replication competent. Therefore, Applicant argues, the cited references do not teach or suggest an RNA viral vector. Additionally, Applicant argues that the cited references also fail to teach or suggest a method of treating a subject having a proliferative disorder as claimed, because they fail to teach or suggest the instant replication competent retroviral vector. Applicant concludes that, since the Examiner did not provide any evidence that the cited references disclose or suggest all the claim elements, and therefore, Applicant requests the withdrawal of the rejection.

Applicant's arguments are acknowledged, however, the rejection is maintained for the following reasons:

Ram et al. teach a method of treating glioblastoma in rats by *in vivo* intratumoral administration of cells producing a replication defective retrovirus comprising all elements recited by the instant claims (see the non-final Office action of 04/10/2007).

Art Unit: 1633

While it is true that Ram et al. do not teach replication competent retroviruses, the art teaches the advantages of using replication competent viruses to treat cancer. For example Martuza and the '096' patent teach that (i) replication deficient viral vectors are unsuitable for treating human tumors because of their inability to completely penetrate into tumors *in vivo* because each replication defective retroviral particle can only enter a single cell and therefore it cannot productively infect other cells and (ii) replication competent viral vectors are needed for efficient therapy because they are able to enter into tumor cells, make copies, lyse the cell and spread to the neighboring tumor cells. Therefore, one of skill in the art would have motivated to modify the method of Ram by making their retroviral vector replication competent. The fact that Martuza and the '096' patent teach DNA viruses is irrelevant. One of skill in the art would have known to apply the concept of replication competent vector to the retroviral vector of Ram et al.

Applicant's argument that one of skill in the art would not have known how to modify a retrovirus in order to make it replication competent is not found persuasive. In order to make a replication defective retrovirus, those of skill in the art must necessarily know what genes are important for replication and which are not (it is noted that this was common knowledge at the time the invention was made). Therefore, those of skill in the art would have known what genes to add back to the vector of Ram et al. to obtain a replication competent virus. Making replication competent retroviral vectors was routine in the art, at the time the invention was made. Therefore, the invention is *prima facie* obvious over the cited references.

Art Unit: 1633

7. Claims 41-45, 49-51, 56, 58, 59, 61, 66, 70, 71, 73, 75, 77-80, 87-92 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Ram et al. taken with Martuza and Martuza et al. (the '096' patent), in further view of both Kuryama et al. (Int J Cancer, 1997, 71: 470-475) and Yan et al. (Prostrate, 1997, 32: 129-139) for the reasons of record set forth in the non-final Office action of 04/10/2007. Applicant's arguments filed 06/08/2007 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that Ram et al., Martuza and the '096' patent fail to disclose or suggest each and every element of the claims, and that Kuryama et al. and Yan et al. do not make up for these deficiencies.

Applicant's arguments are acknowledged, however, the rejection is maintained for the reasons set forth above.

8. Claims 41-45, 49-51, 56, 61, 63-70, 71-73, 75, 77-80, 81, 82, 87, 89-91, 93, and 95 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Ram et al. taken with Martuza and Martuza et al. (the '096' patent), in further view of Kasahara et al. (Science, 1994, 266: 1373-1376) for the reasons of record set forth in the non-final Office action of 04/10/2007. Applicant's arguments filed 06/08/2007 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that Ram et al., Martuza and the '096' patent fail to disclose or suggest each and every element of the claims, and that Kasahara et al. does not make up for these deficiencies.

Applicant's arguments are acknowledged, however, the rejection is maintained for the reasons set forth above.

9. Claims 41-45, 49-51, 56, 61, 63-70, 71-73, 75, 77-80, 81, 82, 87, 89-91, and 93-96 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Ram et al. taken with Martuza, Martuza et al. (the '096' patent), and Kasahara et al., in further view of Kuryama et al., for the reasons of record set forth in the non-final Office action of 04/10/2007. Applicant's arguments filed 06/08/2007 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that Ram et al., Martuza and the '096' patent fail to disclose or suggest each and every element of the claims, and that Kasahara et al. and Kuryama et al. do not make up for these deficiencies.

Applicant's arguments are acknowledged, however, the rejection is maintained for the reasons set forth above.

Conclusion

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the

Art Unit: 1633

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1633

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ileana Popa, PhD

/Joseph Woitach/
Joseph Woitach
SPE 1633